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Medical Department

DIVISION OF EXPERIMENTAL PATHOLOGY

Carcinogenic Action of Graded Doses of Whole-Body Irradiation (6120, 6310)*

The major tumor that has been induced by whole-body irradiation in the lethal and sublethal range is a mammary tumor that varies in appearance from a fibroadenoma to an adenocarcinoma with a few fibrosarcomata. The 1-yr incidence of mammary tumors is dose dependent and extrapolates back to approximately zero dose. The mechanism of induction appears to be indirect and requires the presence of a functioning ovary, but the latter need not be irradiated.

The tumors are in part transplantable. Both autonomous and hormone-dependent tumors exist. The rapidly growing autonomous tumor is clearly a carcinoma. Some tumors are metastasizing upon transplantation.

It may be possible in the near future to provide both autonomous and hormone-dependent mammary tumors for cancer chemotherapy testing programs.

V.P. Bond, R.A. Conard, E.P. Cronkite, J. Furth,** and S.W. Lippincott

Metabolism of Co^{60}-Labeled Vitamin B_{12} in Animals and Patients (6120)

Studies on the distribution and excretion of Co^{60}-labeled B_{12} in dogs and other animals have been completed and reports are being prepared. Further work on plasma clearance and excretion of labeled B_{12} in various blood dyscrasias and "normal" controls has been completed. Plasma concentration curves of Co^{60} after the intravenous injection of the labeled B_{12} show a periodic and an aperiodic component, which indicates that clearance is progressing simultaneously with mixing. The aperiodic portion consists of a fast and a slow component. Curve analyses are under way. Urinary and fecal excretion show two clear components, one with a half-time of 2½ days and the other with a half-time of more than 300 days. The earlier suggestion of fast and slow plasma clearances in various blood dyscrasias must be reconsidered in view of the difficulty of curve analysis in the presence of simultaneous mixing and clearance.

E.P. Cronkite, E. Henley,* L.M. Meyer,** J.R. Rubini, D.A. Willigan, and W. Wolins

Radioautograph Studies of Cell Proliferation in Animals Utilizing Tritium-Labeled Thymidine (6120)

Tritium-labeled thymidine, developed by W.J. Hughes of this Department, has proved to be most effective in labeling the desoxyribonucleic acid (DNA) of proliferating tissues of the mouse. These studies are being made in collaboration with the BNL Biology Department and the National Institutes of Health (G. Brecher). To date the appearance and disappearance of labeled blood cells in the peripheral blood following single injections of labeled thymidine have been followed, as has their appearance in all tissues throughout the body as a function of time. In addition transfusion of labeled leukocytes has been accomplished and promises to be useful in studying the life span and fate of leukocytes. To date it appears that this agent will be most helpful in unraveling various time features of the generative cycle (intermitosis and mitosis).

V.P. Bond, R.A. Conard, E.P. Cronkite, W.L. Hughes, R. Painter, and H. Quastler†

Combined Effects of Beta Irradiation of the Skin and Whole-Body X-Irradiation on Carcinogenesis in the Skin (6310)

The possible additive effects of whole-body radiation and localized beta radiation of the skin in regard to carcinogenesis of the skin have not

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*For explanation of these numbers, see Foreword.

**Research collaborator from Children's Cancer Research Foundation, Boston, Mass.

*Research collaborator from the University of Washington, Seattle, Wash.

**Research collaborator from South Nassau Communities Hospital, Oceanside, N.Y.

†Member of the Biology Department

been determined. The problem is of both theoretical and practical interest, since the Marshallese people who were accidentally irradiated with fallout developed beta lesions of the skin and received a substantial dose of whole-body irradiation.

Groups of 50 female mice have been given 20,000 rep of beta radiation from a Sr^{90} source (750 rep/min) to a flap of skin on the back (area = 0.9 cm^2). Other groups of 50 mice have been given the same beta doses to the skin plus 400 r of whole-body x-irradiation. Still other groups of 50 mice were given 6000 rep of beta radiation to the skin, and corresponding groups received the same beta doses to the skin plus 400 r of whole-body irradiation. Another group of mice have received only a whole-body dose of 400-r x-radiation. Preliminary results indicate that in the 6000-rep group which received in addition 400 r of whole-body x-irradiation there was more skin damage at the site of the beta irradiation than in the group receiving the 6000 rep alone to the skin. A few malignant skin tumors are appearing which have been verified by histological study. The incidence of such tumors in the various groups will be determined in the near future.

R.A. Conard, E.P. Cronkite, and V.P. Bond

Studies on the Toxicity of Irradiated Intestine (6120)

The intestinal syndrome produced by supralethal doses of ionizing radiation is associated with 3- to 5-day deaths in most animals. The syndrome is characterized by extreme toxicity which seems greater than would be accounted for on the basis of fluid and electrolyte imbalance alone. The present studies were undertaken to determine whether any toxic agent (or agents) which might contribute to the syndrome is present in the irradiated intestine.

Many experimental approaches have been tried with, for the most part, negative results. Early toxicity of mucosal scrapings from unirradiated mice when injected intraperitoneally was found to be due largely to sepsis. Lethality from intravenous injections (very small amounts) is thought to be due to potassium toxicity.

Attempts are being made to determine toxicity by a more normal route of injection such as directly into the intestines of irradiated mice. Studies are under way on the influence of an increase in body levels of potassium and sodium (by addition of the elements to the drinking water) o the survival time in the acute intestinal syndrome. An attempt is also being made to protect irradiate mice from the intestinal syndrome by intralume injections of normal mucosal cells into the sma intestine in the hope of producing seeding.

R.A. Conard and H. Quastl

Studies on the Marshallese People Exposed to Fallout Radiation (660

The annual expedition to the Marshall Islands the medical examination of the 82 Marshallese pe ple exposed to significant fallout radiation in 19 was carried out in March 1957, three years a exposure. The findings of this survey will be p lished in a joint BNL – Naval Medical Resea Institute report. Preparations are being made f four-year survey in March 1958. Hematolog and other examinations are contemplated for next survey, which will be made at Rong where these people now live. In addition, hoped that a whole-body gamma analyzer wi set up aboard a Navy LST for the purpose of rying out gamma spectrographic analyses on exposed and unexposed people on Rong These will be correlated with urinary excr rates of isotopes. As in the past, the United S Navy is assisting the Atomic Energy Commis Brookhaven National Laboratory, and agenc the Department of Defense in this survey.

R.A. Conard, B. Cannon,* Col. A. Lowe
J.E. Rall,† Lt. Col. S. Ba
L. Meyer, and E. Ca

Studies on the Therapeutic Efficacy of an Aloe vera Extract in Beta Lesions of the Skin (6

The therapeutic efficacy of local daily ap tion of an *Aloe vera* plant extract to acute burns of the skin of mice and rats is being t Results are inconclusive at this time. The e (furnished by Forkas Chemical Corporat said to be of benefit in the healing of th burns. R.A. C

*Massachusetts General Hospital, Boston, Mass.
**MC USA (Walter Reed Army Medical Center, Was D.C.)
†Research collaborator from National Institutes o Bethesda, Md.

Pathology of Particle Radiation (6310)

Studies are being carried out on the pathological effects of thermal neutrons and of the heavy particles from the $B^{10}(n,\alpha)Li^7$ reaction on the skin of pigs. S.W. LIPPINCOTT, V.P. BOND, J.S. ROBERTSON AND E.P. CRONKITE

Clinical Studies of Labeled Protein Fractions (6310, 6320)

Clinical studies of labeled protein fractions are being carried out on normal individuals, patients with miscellaneous diseases, and patients with various types of carcinoma, as a possible diagnostic aid in detecting early cancer.

S.W. LIPPINCOTT, W.L. HUGHES, W. WOLINS, AND C.T.O. FONG

Function, Fate, and Control of Platelets (6120)

High levels of a physiologically active substance, serotonin, are found in blood platelets and parts of the gastrointestinal tract. Serotonin levels of tissues and platelets will be measured colorimetrically from tissues of normal and irradiated animals and platelet preparations to assess further the role of this substance in radiation injury and the effectiveness of platelet preparations in controlling radiation hemorrhage.

Urine levels of 5-hydroxyindoleacetic acid, the excreted metabolite of serotonin, will be measured in normals, leukemics, and other blood dyscrasias.

In addition, the comparative effectiveness of fresh and lyophilized platelets in the control of radiation bleeding will be evaluated.

V.P. BOND, R.A. CONARD, E.P. CRONKITE, J. RUBINI, AND D. SORENSEN

Papers Presented

FIRST INTERNATIONAL CONGRESS OF NEUROLOGICAL SCIENCES, BRUSSELS, JULY 1957

The Neuropathological and Topographical Study of Whole Brains Following Neutron Capture Therapy in Glioblastoma Multiforme. L.E. Farr, S.W. Lippincott, W. Kahle, P. Yakovlev,* and W. Haymaker.**

FIRST PAN-AMERICAN CANCER CYTOLOGY CONGRESS, MIAMI, APRIL 1957

Studies on Tissues of Animals Receiving Sulfur-Labeled Platelet Transfusions. E.P. Cronkite.

AMA FIFTH ANNUAL NATIONAL CIVIL DEFENSE CONFERENCE, NEW YORK, JUNE 1957

The Effects of Total-Body Exposure to Ionizing Radiation on Human Beings – Fallout Problems and Civil Defense. E.P. Cronkite.

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*Research collaborator from Harvard Medical School, Boston, Mass.

**Research collaborator from Armed Forces Institute of Pathology, Washington, D.C.

Publications

Prepared statement on Somatic Effects, testimony before Joint Committee on Atomic Energy, Congress of the U.S., June 3, 1957, at the open hearings on The Nature of Radioactive Fallout and Its Effects on Man. E.P. Cronkite. *Congressional Record*, September 1957.

Fallout, Civil Defense and Effects of Radiation on Man. E.P. Cronkite. *J. Am. Veterinary Med. Assoc.*, in press.

The Use of Platelet Transfusions in Hemorrhagic Disease. E.P. Cronkite and D.P. Jackson.* Chapter in *Progress in Hematology*, Grune and Stratton, New York, 1957.

Gastric Lesions in Experimental Animals Following Single Exposures to Ionizing Radiations. G. Brecher,** E.P. Cronkite, R.A. Conard, and W.W. Smith.† *Am. J. Pathol.*, in press.

Acute Whole-Body Radiation Injury: Pathogenesis, Pre- and Postradiation Protection. V.P. Bond, E.P. Cronkite, and R.A. Conard. *Atomic Medicine*, in press.

The Diagnosis and Therapy of Acute Radiation Injury. E.P. Cronkite, V.P. Bond, and R.A. Conard. *Atomic Medicine*, in press.

The Hematology of Ionizing Radiation. E.P. Cronkite, V.P. Bond, and R.A. Conard. *Atomic Medicine*, in press.

Fallout Radiation: Effects on the Skin. R.A. Conard, E.P. Cronkite, and V.P. Bond. *Atomic Medicine*, in press.

Human Radiation Injury Diagnosis, Therapy and Prognosis. E.P. Cronkite. *Proc. 6th Intern. Congr. Hematol.* (Boston), 1957.

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*Research collaborator from the Johns Hopkins University School of Medicine and Hospital, Baltimore, Md.

**Research collaborator from National Institutes of Health, Bethesda, Md.

†National Institutes of Health, Bethesda, Md.

DIVISION OF MICROBIOLOGY

The Sites of Catabolism of Plasma Albumin (6120)

In an extension of the study reported a year ago (W.L. Hughes, *Proc. 8th Ann. Conf. Natl. Nephrosis Found.*, 1956, p. 22) on the effect of nephrectomy on the catabolic rate of labeled plasma albumin, the effect of removing the intestines or large portions of the liver has been investigated. Removal of the intestines had no effect, but removal of portions of the liver decreased the rate of catabolism in proportion to the amount of liver removed. This effect can be much greater than that seen following nephrectomy and suggests that the liver must be the major site of catabolism for plasma albumin.

D. Gitlin,* J.R. Klinenberg,** G. Terres, and W.L. Hughes

Catalobism of Serum Albumins in Mice (6120)

The comparison of data obtained in this laboratory for the half-life of crystalline bovine serum albumin (BSA) with the data for human serum albumin (HSA) reported by Melcher et al. [*J. Immunol.* 71, 275 (1953)] shows nearly a twofold difference. These investigators, using iodinated HSA and following the catabolic rate by serum sampling, have found a half-life of 1.5 days. At BNL, by using whole-mouse counting, the biological half-life for iodinated BSA has been found to be between 0.6 and 0.7 days. Although it would be surprising if mice could distinguish between HSA and BSA to the extent noted (short of an immune response), various preparations of HSA (crystalline, fraction V, and commercially prepared RISA) were tested in BNL mice with whole-body counting. The results indicated no significant difference in half-lives between the different HSA preparations; they had half-lives of 0.75 days, slightly longer than those for BSA. Further studies in which the catabolic rate was determined both by whole-mouse counting and by serum sampling ruled out the possibility of differences based on methods of determination. Since it is felt that Melcher's group has reported an accurate value, and that the results obtained at BNL also merit confidence, the present line of investigation is being continued in an attempt to resolve this discrepancy. The approach now being followed is one of testing various strains of mice. G. Terres and W. Wolins

An Investigation of the Induction of Acquired Tolerance to Crystalline Bovine Serum Albumin in Mice (6120)

To date all work with mice on acquired tolerance homotransplantation resulting from prenatal exposure of the same homologous tissue. This procedure was unsatisfactory for studies in which large numbers of animals were desired, since a high mortality rate occurred. Recently Billingham and Brent [*Proc. Roy. Soc. (London)* B146, 78 (1956)] have reported a higher occurrence of tolerant animals when the inducing exposure is made at birth and intravenously. The work with tissue still has the disadvantage of involving a heterogeneous mixture of antigens, with each antigen establishing its own state of tolerance in accordance with its own essential characteristic properties. As a step toward the elucidation of the mechanism underlying tolerance, a system employing a pure antigen and capable of easily producing a state of tolerance in a large number of animals seemed highly desirable.

Crystalline bovine serum albumin (BSA) was chosen as the antigen to be tested, and postnatal injection as a possible method of induction. The initial injections of BSA (12.5 mg in 0.05 ml) were made intraperitoneally. Very few mice were lost as a result of the method of injection. This procedure was tested in single and multiple exposures at various periods after birth. Animals so exposed were later given a series of sensitizing injections to test for the establishment of tolerance. The procedure of sensitization was such as to produce fatal anaphylaxis in 40 to 75% of control mice.

The most successful experiment resulted from initial exposure to 4 injections starting at birth or at 1 wk of age and administered on a 1-3-6-8-day schedule. The mice were tested for tolerance at 6 wk; none of the treated mice showed any signs of shock, while the controls (litter mates) showed approximately 40% fatalities. The same procedure was tested when the mice were 11 and 17 wk of age. Fatal shock was recorded in the treated animals, but less frequently than in the controls, which indicated a transient characteristic. Animals given a single exposure also showed less anaphylaxis than the controls, but the differences were less significant.

Postnatal exposure to greater amounts of BSA produced an effect even when the mice were 6 mo of age. The amount used per injection in the post-

as well as hydroxylysine, during 2 wk was unexpected, as collagen is believed to have practically no turnover.

The increase of the ratio of the C^{14} activity of hydroxylysine to that of lysine in the collagen was related to time in a manner which made it doubtful that the increase occurred after incorporation of the C^{14}-lysine into the collagen. If hydroxylation followed the incorporation of lysine into the collagen gradually and in 1 hr reached 68% of its theoretical limit, it would be expected, with allowance for the rate of lysine incorporation, that after 4 hr the C^{14} activity of the hydroxylysine would rise from 68 to about 95% of that of the lysine, whereas the rise was only to 70%, 100% being reached only in the 2-wk experiment.

One possible explanation is that the collagen prepared from skin by present methods contains two or more proteins. One of these is collagen with a relatively slow turnover, which hydroxylates part of its lysine at the moment of incorporation. The other protein or proteins incorporate lysine without hydroxylating any of it and have a relatively short half-life, so that in 2 wk or less they disappear with their lysine, leaving collagen with equal C^{14} activity in lysine and hydroxylysine.

In the 2-wk experiment the observed difference of 9% in C^{14} activity between lysine and hydroxylysine, the latter being greater, appears to be outside the limit of experimental error, and is one of the results that await confirmation and explanation. The problems raised by the above results will be further studied. D.D. Van Slyke and F.M. Sinex

DIVISION OF PHYSIOLOGY

Basic Physiology of Manganese (6120)

Development of neutron activation methods for the determination of manganese in biological materials in which its concentration is very low has been postponed because of the temporary unavailability of certain necessary equipment. Preliminary evaluation of new analytical apparatus is anticipated for the coming quarter, however.

D.C. Borg and L. Grodzins*

Pilot studies have been completed on the application of electron magnetic resonance techniques to the measurement of tissue manganese and the determination of its valence state *in situ*. At present the sensitivity of this method appears insufficient for application to most biological samples; however, certain alterations in the magnetic spectrometer and proposed changes in the sample preparation procedures will permit a re-evaluation of this approach within the next several months.

D.C. Borg, G.C. Cotzias, and M. Birnbaum*

Human Manganese Metabolism (6120, 6320)

Metabolic studies with radiomanganese tracers in humans have progressed to the first study of long-lived radioisotope (Mn^{54}) metabolism in patients. Data currently being gathered and evaluated indicate that employment of this isotope will be profitable and may allow correlation of human studies with animal experiments previously reported. D.C. Borg and G.C. Cotzias

Extracerebral Factors in the Transfer of Sugars Between Blood and Brain (6310)

After preliminary trials with other mammalian species, a relatively simplified perfusion circuit has been evolved for the isolated cat brain. The circuit utilizes the intact lung *in situ* for oxygenation and filtration. This adaptation of existing surgical technique includes per-cardiac catheterization of the pulmonary circulation with polyethylene tubing. Early trials of various shapes and sizes of tubing proved inclusion of the lung in the perfusion circuit feasible. Separation of the pulmonary from the systemic circulation via intracardiac shunts has been demonstrated by dye injections. The importance of effective closure of the extradural cerebral venous channels was similarly shown. The anatomic peculiarities of the only site where such complete separation can be made between the cerebral and the polyanastomotic vertebral venous sinuses dictated an improved method of closure. Ligatures, special clamps, a mechanical screw obturator, and electrocautery fulguration with different electrodes were tried. A combined technique was developed which involved a relaxing incision, partial cranial disarticulation, preliminary circumferential extradural ligation of the spinal cord, and final permanent occlusion with soft wire. The postligation integrity of the cerebral venous sinuses has been demonstrated with dye injections. During dye injections into the apparently completely isolated cerebral circulation, it was noted that a lessening of pressure of perfusion

*Member of the Physics Department.

brought about a resurgence of undyed blood into both injected and ejecting tubing, which indicated an expansile nonmixing compartment in the cat's cranial vascular system. Cerebral angiography (done with the assistance of H. Bagnall) demonstrated the patency of the anastomoses between the cerebral hemispheres. Additional dye injections showed that such an expansile, nonmixing vascular compartment was present if the contralateral carotid artery and external jugular vein were ligated prior to perfusion. The necessity for bilateral arterial and venous cannulation in projected experiments with radioactive tracers was indicated.

The need for continuous arterial flow to the brain prior to perfusion and the desirability of simultaneous recording of anoxic and hypoglycemic states will probably necessitate the use of electroencephalographic methods of recording.

An effective adaptation of a perfusion pump has been made, after trial of several types, on the basis of adequate flow, dependability, and separation of perfusate from the mechanism. The latter feature obviates clot formation and radioactive contamination of the pump.

Further development of the isolated cat brain-lung preparation will include increased speed of preparation, synchronization of perfusion with tissue demands, development of suitable perfusate, adaptation of electroencephalographic recording, selection of anesthetic, and sundry mechanical improvements.

P.G. LeFevre and G.F. McGinniss

The Role of Carbohydrate and Mineral Metabolism in Control of the Cerebral Excitatory State (6120)

The importance of the nature of the substrate in regard to the inhibiting action of the antihistamine drugs on the respiration of rat brain cortex slices is being investigated by Warburg respirometry. Preliminary trials have not verified certain specific distinctions reported by others.

P.G. LeFevre and G.F. McGinniss

Active Transfer of Metabolites Through Cell Membranes (6120)

Interest continues to center on the steric specificity of the monosaccharide carrier system in the human red cell membrane. Although the widely differing carrier affinities of the various sugars do not seem to follow a consistent pattern in relation to molecular configuration, a distinct relation has been established between these ities and the pyranose conformational stabil of all available aldohexoses and aldopento This correlation is such as to imply that the C1 f may be essential in the substrate if it is to m use of the carrier. An apparent complication application to the ketohexoses may reflect rather high furanose component in aqueous so tions of these materials. The extent of the gener ity of the conformational correlation is being in vestigated with some of the rarer sugars obtain from private sources; however, the most critic test-sugars have not become available, and syn thesis is currently being attempted.

The striking competitive inhibition of this sys tem observed with phloretin (the aglucon of phlorizin) has led to comparative study of compounds of similar structure. Since even the largest fragments of phloretin tested have shown far less inhibitory activity than the complete phloretin molecule, it is suggested that at least two points widely separated on the unfolded molecule (probably at the hydroxyl groups) are involved. Current investigations with a number of homologues and substituted derivatives are expected to narrow the possibilities as to the active sites. Further attention is also being directed to the equally phloretin-specific reversible attachment of the agent to the erythrocytes, as demonstrated chemically. Preliminary observations on the mouse Ehrlich ascites tumor indicate that these cells (which have a hexose transport system comparable to that of human erythrocytes) also exhibit great capacity for accumulating phloretin from the medium.

P.G. LeFevre and J.K. Marshall

Studies of Viability of Mouse Brain Tumor Following Boron-10 Neutron Capture Irradiation (6310)

The viability of mouse brain tumor following the administration of sodium pentaborate decahydrate (enriched with B^{10}) and neutron capture irradiation has been studied in the following manner: Each animal of a group of mice received a tumor transplant which was allowed to grow for approximately two weeks. The mice were then divided into four groups. Group A (RNI) was exposed to thermal neutrons; Group B (INR)

ived only an injection of B^{10} (sodium penta-**ate** decahydrate); Group C (NIOR) was given **treatment**; and Group D (IR) was injected **h B^{10}** and then exposed to thermal neutrons. **mediately** after treatment all the mice were sac-**ed, and** the tumor tissue from each was trans-**ated** into ten normal recipient mice. Data on **tality** due to tumor growth and on longevity **e then** collected during a 60-day observation **od.** (These mice received no further treatment.) **eral** levels of B^{10} and thermal neutron doses **re** employed. In Figure 1 are presented the **lts** of these experiments. These results indicate **t treatment** with B^{10} plus thermal irradiation decreases tumor viability, since transplants from mice treated in this way (Group D) caused a much lower mortality among the recipients.

L.E. Farr, T. Konikowski,
and O.D. Easterday

Boron Toxicity in Mice **(6310)**

Studies are being continued in which the toxicity of various complexing agents of the carbohydrate group is under investigation. Approximately one half of the agents chosen for examination have been screened. The data are being subjected to probit analyses and relative potency evaluation.

O.D. Easterday

NIOR = NEITHER INJECTED OR RADIATED
RNI = RADIATED NOT INJECTED
INR = INJECTED NOT RADIATED
IR = INJECTED AND RADIATED
Y = 2 GROUPS IN DOUBT INCREASE PERCENT MORTALITY 3.3 %

DRUG: SODIUM PENTABORATE DECAHYDRATE (B^{10}) 1 MOLE + 0.5 M. GLUCOSE

	CONTROL								IRRADIATED 10 MINUTES AFTER INJECTING B^{10}							
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
E	NIOR	RNI	RNI	INR	INR	INR	INR	INR	IR	IR	IR	IR	IR	IR	IR	IR
NVT cm^2		8×10^{11} 9.4×10^{11}	1×10^{12} 1.4×10^{12}						8×10^{11} 9.4×10^{11}	8×10^{11} 8.9×10^{11}	1.3×10^{12}	8×10^{11} 8.9×10^{11}	1×10^{12} 1.4×10^{12}	8.7×10^{11} 9×10^{11}	1×10^{12} 1.4×10^{12}	9.22×10^{11}
B/gm wt				100	150	175	200	250	100	150	150	175	175	200	200	250
ERAGE DEATH	14	14.5	15.5	15	12.5	15.5	17	16.5	*25*	*28.5*	*30*	*28.5*	*29*	*33*	*38.5*	

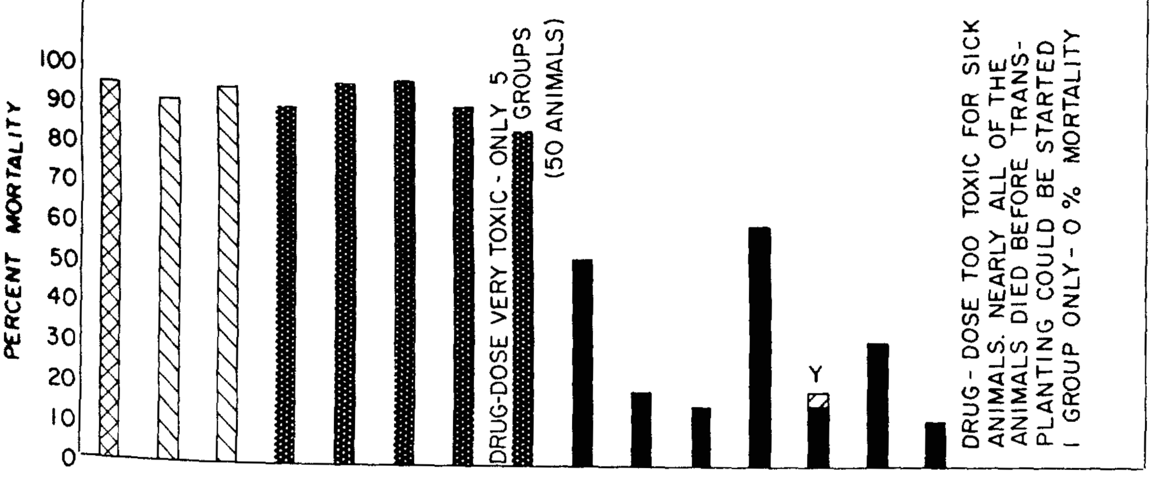

Figure 1. Results of mouse tumor radiation experiments, based on 10 groups of 100 animals each, 60-day observation time.

Organo-Boron Toxicity in Mice (6310)

The determination of solubilities for a number of organometallic compounds, including organic boron, is in progress. These studies will be followed by toxicity investigations in mice.

O.D. EASTERDAY

The Experimental Application of Neutron Capture Therapy to Glioblastoma Multiforme (6310)

Studies are being continued on the experimental application of neutron capture therapy to glioblastoma multiforme neoplasms. Six patients have each received neutron irradiation over a 10-min period during which continuous constant flow infusion with sodium pentaborate decahydrate was carried out. The route of administration was via the ipsilateral internal carotid artery. There has been no evidence of serious scalp reaction or other complications of note in these six patients. Additional patients will be admitted in the near future to broaden the scope of these studies.

Experimental methods are being established by which the blood volume in neoplastic and in normal tissues in mice may be compared.

L.E. FARR AND H.J. BAGNALL

Nomogram for the Calculation of Total Beta and Gamma Dose Rate (6120)

A nomogram has been developed by means of which almost instantaneous calculation can be made of the dose rate for all the biologically important isotopes, provided that an estimate is available of the weight of the patient, animal, or organ for which this value is sought.

A. BERTINCHAMPS

Determination of Vascular Volume in Normal and Neoplastic Tissue by Use of Suitable Radioactive Isotopes as Labels of Vascular Components (6120)

Chromium, phosphorus, and tritium are at present being used as labels. Preliminary studies are necessary to establish conditions whereby either reproducible blood volumes or an estimate of deviation from the mean can be obtained; and to determine the influence of the sacrificial method and the handling of the specimen on the results.

H.J. BAGNALL

Publications

Radioactive Isotopes in Parentera
Cotzias. *Bull. Parenteral Drug Assoc.* 11

DIVISION OF MEDICAL

Radiation Dosimetry

Isotope Comparator. A precision isotope comparator w
general use with routine materia
ment an air ionization chambe
electrometer circuit for the rate-
ment procedure. A second instru
pleted for evaluation of flat beta
sources in which use is made of a
chamber of Failla's design previo
Instrumentation Division.

In Vivo Radioactivity Scanner. Efforts are being continued to mo
commercial *in vivo* radioisotope s
provide the precision and dependa
at BNL. Further electronic and
provements are required before s
formance can be achieved.

Beta Applicator Calibration. A report has been completed on thi
Of most interest is a description of
Y^{90} beta applicator, calibrated wi
lation ionization chamber and by
clear film. Surface and depth dos
by the two methods were in good
use of a polystyrene phantom, the s
found to be 26.2 esu/cc-sec or 1430
an estimated accuracy of $\pm3\%$. T
thickness was determined to be 0.1

Radiation Detection and Analysis. Pulse height analyzer techniques
plored for use in activation analysi
neous multiple isotope tracer stu
equipment has been modified to ap
service desired for this work, as an a
ing the design of more suitable circu

J.S. ROBERTSON AND I

Whole-Body Burden of Radioactivity. A study of the whole-body burden
for natural and accidental radioac
is under way, in view of interest in t

lem here and in cooperation with the continuing study of the Marshallese population.

J.S. ROBERTSON AND E.E. STICKLEY

Chemical Dosimetry (6120)

This work was initiated as a contributing phase in the energetic heavy particle (neutron capture) radiation studies, as well as for its usefulness in gamma-ray and other applications. Development is concomitant with those biological projects with which it is directly associated. V.P. BOND AND E.E. STICKLEY

Development of the Use of Europium-155 in Portable Diagnostic X-Ray Devices (6120)

A series of radiographs has been made, the source being about 5 mC of Eu^{155} prepared by activating 100 mg of Sm^{154} in the BNL research reactor. A second source, activated at the MTR, was broken during transfer for shipment. The 5-mC source was used by placing it in a shutter designed for use with similar Tm^{170} sources which was kindly lent to BNL by the Army Medical Equipment Development Laboratory, Fort Totten, N. Y. Because of the low activity of the source relative to that required in an operational device, the exposure times have necessarily been very long (hours to days), and it has not been feasible to use human beings as subjects. Radiographs of metallic objects, isolated bones, and a leg of lamb, however, indicate that a satisfactory degree of contrast and good resolution can be obtained with Eu^{155}. As has been the case with Tm^{170} sources, the quality of the radiographs is inferior to that obtainable with a good x-ray machine, but is satisfactory for projected field uses.

Investigation of the separation of Eu^{155} from Sm has continued. The use of cation exchange columns appears to be unsatisfactory, but other column methods are being tried. J.S. ROBERTSON

Cobalt-60 Source (6120)

Isotopes Used in Tracer Studies (6120, 6310, 6320)

The use of several isotopes is being developed in the Department by members of other divisions. The Medical Physics Division participates in these developments by providing the necessary instrumentation for the special problems as they arise, and by providing consultation service.

Projects in hematology have been begun on the application of Co^{58} as well as Co^{60}, along with Fe^{59} and Cr^{51}-labeled compounds, separately and in combination. The isotopes Mn^{52}, Mn^{54}, and Mn^{56} continue to be used in research studies of diagnostic and therapeutic interest. Attempts are still being made to develop the Ca^{47} isotope, because of its great potential value in a wide variety of research fields; reactor production from enriched Ca^{46} and cyclotron activation from Ca^{48} are possible approaches. Mg^{28} has been used for many studies but the specific activity available, either from reactor or cyclotron production methods, precludes valid results *in vivo*, since the carrier burden of magnesium is still so great that interfering pharmacologic effects are produced.

E.E. STICKLEY AND J.S. ROBERTSON

Reactor Neutron Beam Evaluation (6120, 6310)

A new series of neutron comparison measurements was made for standardization purposes by using the tissue-equivalent ionization chamber in the medical facility and in the biology facility at the reactor. This instrument was also used in the middle energy neutron experiments on mice at the small cyclotron. Standardization under x-ray was also included in the series.

The probe ionization chamber, guard-ring type, has been modified for application in the present reactor medical facility. X-ray testing and calibration have been carried out for both the graphite and tissue-equivalent electrode arrangements in pressure measurement, gas storage, and mixing. At the present stage of development a variety of accessory instruments can be used to measure the ionization current output, depending on the radiation level of the field in which measurements are being made. This instrument is designed to provide differential measurements of the several components present in the mixed radiation pattern characteristic of reactor exposures. It is provided with a remote manipulating device for scanning within liquid phantoms under exposure conditions.

Newly acquired electrometers were tested with the ionization chamber and gamma sources. Three electrometers have given evidence that they may produce reliable measurements when used with the ionization chamber. After calibration of the tissue-equivalent ionization chamber with a strong gamma source, the apparatus will be ready for use in thermal neutron dosage studies.

R.I. Weller and E.E. Stickley

An immediately practical study of neutron flux patterns for the brain tumor neutron capture experiment has been begun by using the gold wire activation technique in a phantom constructed within a human skull. Simulation of skin and brain tissues is being developed in order to provide the most accurate picture possible of the neutron flux density at internal positions of greatest interest, in terms of both desired treatment regions and regions where protection is of critical importance.

E.E. Stickley

Medical Research Reactor (6120, 6310, 6320)

Construction of the medical research reactor has reached the stage of heavy concrete pouring for reactor and treatment-room shielding. Electronic components have been completed and delivered; they are being tested by use in circuits of the Brookhaven research reactor. The aluminum reactor tank and shield liner have been delivered, as have the shutter assemblies. Graphite fabrication was completed in BNL shops and the 700 pieces were test-assembled. Control rod drives have not been finished; the contractor is now refining their design.

Since the reactor itself is well on the way toward completion, design effort is directed toward detailing plans for accessory apparatus which was presented in conceptual form only in the early phases of the planning program.

E.E. Stickley

Biological Effects of the Energetic Heavy Particle Radiation From the Neutron Capture Reaction (6120, 6310)

Weight Loss. Studies of rbe using spleen-thymus weight loss have been completed and a report has been published. Studies using mortality as the criterion of effect have also been completed and a report has been written. The rbe for recoil particles from B^{10}, Li^{6}, and U^{235} has been determined by using testis weight loss and a report is in preparation. Additional studies to determine the effect of boron dose on the degree of response are in progress.

V.P. Bond

Pathology. The rbe of heavy particles from the $B^{10}(n,\alpha)Li^{7}$ reaction and the pathological effects of these particles on swine skin have been determined, and a report is being prepared.

V.P. Bond

Carcinogenesis. Initial studies on carcinogenesis from the heavy particles liberated in the $B^{10}(n,\alpha)Li^{7}$ reaction had to be terminated after eight months because of a severe mite infestation in the C-57 mice being used. A second experiment using CF-1 mice is now under way.

V.P. Bond

Recovery. Initial studies on the rate of recovery of mice from heavy particle irradiation have been completed and the results have been presented. Additional studies will be initiated when time and personnel become available.

V.P. Bond, O.D. Easterday, and E.E. Stickley

Tracer Theory (6120)

An analogue computer is being constructed for the Medical Department by the Instrumentation Division. The existing analogue computer is being used by the Physiology Division (D.C. Borg) in the analysis of data on manganese metabolism.

J.S. Robertson

Water and Electrolyte Exchange: Halide Metabolism (6120)

During the quarter analysis of data from experiments already completed was the principal activity in this field. Design of further experiments will be postponed until this phase has been completed.

J.S. Robertson

[redacted]

-Body Irradiation (6320)

e patient has been given Na^{24}, as previously ted. Plans to repeat treatment of the first ıt and to extend the series are under discussion.

J.S. ROBERTSON, W. WOLINS, E.P. CRONKITE, V.P. BOND, J.J. NICKSON,* H.H. BANE,* AND A.S. GLICKSMAN*

s Using Light Scattering: ı Interactions (6120)

· study of protein-protein interactions is continued on two specimens, primarily by of light scattering.

ary Mucoprotein. The urinary mucoprotein ım and Horsfall was prepared by the meth- V.M. Di Ferrante. This preparation has ıhibiting activity but aggregates in potas- ıosphate buffer pH 6.8, $\mu=0.046$, although ıble in distilled water.

t-scattering studies of this mucoprotein in ı water reveal marked evidence of molecu- ·action (the Zimm plot is much distorted). ·r, it has been possible to determine a ıar weight of approximately 1.5×10^6 by lation to zero angle, where both internal ·rnal interference effects vanish. This fig- · be somewhat low. The dissymmetry is h at infinite dilution, in keeping with the symmetric nature of the molecule. This that the molecule stiffens somewhat at · ionic strength, but it has not yet been to make this statement quantitative. At ıncentrations, the dissymmetry decreases becomes less than unity, in keeping with ·y of Doty and Steiner (developed for erical molecules).

·v of the difficulty of interpretation of ıts in distilled water, two light-scattering e made in phosphate buffer pH 6.8, which is the highest concentration at e mucoprotein prepared in the present emains stable. The data are consistent ı the above interpretation.

ıcoprotein does not fluoresce in either the ly dispersed or the aggregated state. The ıtion is small but not negligible.

ıy studies with an Ostwald viscometer ed water solvent reveal an intrinsic viscosity of 224.0 by extrapolation which is linear over the four lowest concentrations examined. This again suggests a very asymmetric or rather stiff molecule, although the electroviscous effect undoubtedly contributes to the viscosity. The optical density varies linearly with concentration of mucoprotein in the entire range examined. The refractive index difference also varies linearly with concentration. The ultraviolet absorption spectrum reveals the major protein peak at 277 mμ. Three shoulders appear on the major peak, one at 260 mμ, which may be due to nucleic acid, and two unexplained shoulders at 283 and 291 mμ. The pH is below 6.0. An attempt is now being made to examine this mucoprotein in as concentrated a buffer as possible.

Hemocyanin From Squid. In collaboration with A.B. Barr,* hemocyanin from giant Chilean squid (length = 6 ft) was studied.

Hemocyanin exists only as whole or as half molecules in the pH range studied (6.0 to 10.0). Only whole molecules are found in crude squid blood. Dialysis to acetate buffer at the same pH, $\mu=0.1$, is accompanied by the appearance of half molecules in the ultracentrifuge. Lowering the pH favors the association of the hemocyanin, but dilution favors the dissociation. A pH could not be found at which a dilution series could be run showing only associated molecules and no precipitate. Half molecules alone are stable at pH 10.0 and are suitable for study. By extrapolation to infinite dilution, the sedimentation constant of halves is 11.4 svedbergs. The approximate diffusion constant (one run) is 2.6×10^{-7} cm^2/sec. These data yield a molecular weight of about 4×10^5 for halves and, therefore, 8×10^5 for wholes. The approximate sedimentation constant for wholes is consistent with dissociation into halves rather than quarters.

Titration curves show a considerable increase in charge of the hemocyanin as it dissociates. Blocking SH groups with methylmercury bromide had no effect on association.

Most interesting in terms of protein-protein interaction is the ultracentrifuge pattern at intermediate pH, where both wholes and halves are present. Two peaks appear with an elevated base line between them. The sedimentation velocities

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*Summer student (1957) from George Washington University, Washington, D.C.

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of the peaks are closer together than would be expected from data on pure solutions. In other words, the molecules in these solutions are rapidly associating and dissociating. However, they are not doing this with sufficient rapidity to produce a single peak in the ultracentrifuge. This is a region in which theory is inadequate. M. MAXFIELD

Tissue Culture (6120)

Studies on the dynamics of cell proliferation in the mouse, using tritium-labeled thymidine, have been initiated in conjunction with the Divisions of Pathology and Microbiology. To augment these studies, tissue culture of hematological cells has been initiated. The procedure not only promises to be a valuable research tool, but is of aid in clinical diagnosis of blood dyscrasia as well.
V.P. BOND AND E.P. CRONKITE

Uptake of Tritium-Labeled Thymidine by Embryonic Tissues (6120)

CF-1 mice at various stages of pregnancy have been injected with tritium-labeled thymidine, and the embryos have been sectioned and prepared for autoradiography. This work is a joint project with Yeshiva University. V.P. BOND, M. ATLAS,* AND E.P. CRONKITE

Recovery of Fish From Irradiation (6120)

Preliminary work has indicated that an initial sublethal exposure increases the survival time and probably the LD50 of goldfish. Experiments are under way to verify and extend these observations. This work is a joint project with Columbia University. A. GORBMAN** AND V.P. BOND

Rbe of Low Energy Monoenergic Neutrons (6120)

Data on the rbe of fast neutrons in the region of 100 to 1000 kev are much needed. Preliminary work has indicated the feasibility of performing such studies with the 18-in. cyclotron at BNL. This work is a joint project with Columbia University. V.P. BOND, E.E. STICKLEY, AND H. ROSSI**

*Research collaborator from Yeshiva University, New York, N.Y.
**Research collaborator from Columbia University, New York, N.Y.

Essential Fatty Acid Deficiencies in Swine (6120)

Fatty acid deficiency induced in swine results in dermatosis resembling psoriasis in human beings. These lesions are being studied for pathology, fatty acid and cholesterol metabolism, and distribution of C^{14}-labeled unsaturated fatty acids.
D.K. SORENSEN AND L. GIDEZ

Bone Marrow Function of Irradiated Dogs (6120)

Dogs given nonuniform irradiation have been studied at various intervals following exposure to determine the degree of bone marrow function in the heavily and lightly irradiated regions. Pathology and radioactive iron uptake were used as criteria of function. This work is a joint project with Boston College. V.P. BOND, J. FLAVIN,* AND E.P. CRONKITE

Nevada Field Work (6600)

Depth dose measurements in human sized phantoms were obtained at one nuclear detonation at the Nevada proving ground. These gamma and neutron measurements are now being confirmed and extended. This work is a joint project with the Naval Medical Research Institute.
V.P. BOND, E.P. CRONKITE, AND E.E. STICKLEY

Publications

Bacteriological Studies on Mice Exposed to Supralethal Doses of Ionizing Radiation. I. Radiation From a Nuclear Device. M.S. Silverman,* V.P. Bond, V. Greenman,* and P.H. Chin.* *Radiation Research* 7, 270 (1957).

*U.S. Naval Radiological Defense Laboratory, San Francisco, Calif.

DIVISION OF INDUSTRIAL MEDICINE

Comments on Experience with Emergency Treatment of Hydrofluoric Acid Burns (†)**

On May 15, 1957, while a pilot study in which natural uranium was being dissolved in a closed system was in progress at the Hot Laboratory, one of the pumps exploded unexpectedly and sprayed a hot liquid mixture of F_2, BrF_3, Br_2, U, and UF_6 into the room in which four men were working. Three of the men received only minor burns, but

*Research collaborator from Boston College, Boston, Mass.
**For explanation of this symbol, see Foreword.

he fourth, who was closest to the point of the ex-
losion, was severely injured.

This man was sitting facing a panel board with
is back to the pump bank when he heard a small
xplosion. He got up and started running from
ie room when a second, larger blast occurred,
id he fell or was blown to the floor. At this time
felt pain in his back from the spray of the hot
iuid mixture. Turning partially, he saw flames
ming out of the slug feeler. He got up and ran
tside the building, where his shirt was ripped
. He was not given a shower immediately but
s put into a car and driven to the clinic, a dis-
ice of about 1½ miles. On the way he began to
ice hazing of his vision. At the clinic he was
nediately put into a shower and his eyes were
hed with water.

\ blue-white opacity of both corneas and burns
he skin of his scalp, face, posterior portion of
<, posterior and lateral portions of both upper
lower arms, back to the waist line, and both
les were present. He was given morphine sul-
gr ¼. The skin was washed with saturated
nesium sulfate and a boric acid – borax solu-
containing 1 part borax, 1 part boric acid,
22 parts water. He was admitted to the hos-
where he was placed in bed with continuous
oric acid – borax soaks. Blood was drawn for
ig and cross-matching and for hemoglobin
ematocrit determination. A positive pressure
n apparatus was set up in the room. Serum
iin was obtained and four tourniquets were
it the bedside in case of sudden pulmonary
i. Tetanus antitoxin 1500 u were given after
itive skin test, as was 0.5 ml of tetanus tox-
ne ml of combiotic was given intramuscu-
A lesion on his left wrist where his watch
en was infiltrated with calcium gluconate.
hr a magnesium paste was substituted for
ic acid – borax solution because of the pos-
of boron toxicity from absorption through
ge area of damaged skin if prolonged soaks
ed. About 12 hr after discontinuation of
ks the blood boron level was reported as
per liter of blood.

lrops of tetracain, cortisone, and calcium
ite were instilled in both eyes every hour,
pupils were dilated with atropine.

g the night he vomited. Since no pulmo-
ma had developed, the next morning he
was given 100 ml of isotonic saline with 5% glucose intravenously and one injection of ACTH gel 60 u.

He was given ascorbic acid 200 mg and one polyvitamin capsule three times a day. A lesion on the left ankle that corresponded in severity with the one on the hand was treated with Vitamin A & D ointment. He developed pain in this area and the ointment was discontinued after one day because it was reported that equipment in the accident area with oil or grease on it was corroded to a much greater extent than the clean metal. This lesion became infected and was much longer in healing than the one on the hand.

The estimated total burned area on the day of the accident was more than 50%. By the next morning it was obvious that much of the burn was only first degree. The areas of skin covered by a double thickness of clothes, such as the shoulder straps, had received almost complete protection. This was believed due to the fact that the liquid spray had not soaked through to the skin in these regions.

The patient was treated by exposure to air. The morning after the accident he was dressed in a sterile scrub suit and sterile socks. The sheets on the bed were sterilized and isolation technique was carried out in his room. The lesions dried and crusted over with only a minimum amount of weeping. He was allowed up and about in his room and at night slept on his abdomen to avoid pressure on the back lesions. No shock developed and the blood electrolytes remained within normal limits.

By the second day the clouded external layers of the corneas had sloughed off and he was able to distinguish fingers held in front of his face. Both corneas healed rapidly and vision returned to normal. There was a slight haze of the right cornea which was treated with 1% dionin eye drops.

In spite of daily injections of penicillin the patient developed a few infected areas that were treated locally with Bacitracin ointment. He was discharged from the hospital on the 22nd day after the accident, and subsequent follow-ups were done in the clinic. By this time there were only a few small areas that had not healed. On the 27th day he returned to work.

His daily urine output was collected and uranium analyses were done by the Analytical Sec-tion of the New York Operations Office of the AEC. A continuous elimination rate of 50 μg or more is considered an overexposure. The patient's urine for the first day was about ten times this level but the elimination was quite rapid, falling below 50 μg by the fourth day.

Uranium Levels of Urine

Date	mg U	Volume in ml
5/15/57	0.54	3250
5/16/57	0.12	3100
5/17/57	0.072	2100
5/18/57	0.028	1900
5/19/57	0.020	2100
5/20/57	0.020	2005
5/21/57	0.014	1824
5/22/57	0.017	1466
5/23/57	0.013	1324
5/24/57	0.009	1750
5/25/57	0.008	1750
5/26/57	0.005	1900
5/27/57	0.005	1850
5/28/57	0.005	1950
5/29/57	0.007	1823
5/30/57	0.003	1888
5/31/57	0.003	1956
6/ 1/57	0.003	1644
6/ 2/57	0.003	2054
6/ 3/57	0.004	1641
6/ 4/57	0.004	
6/11/57	0.002	
6/18/57	0.002	

It is not known what portion of the uranium was absorbed through the skin and what portion entered the body through the lungs. However, since this man was in the room for such a short time it is probable that the major portion was absorbed through the damaged skin.

Urinalyses were done on five other people involved and insignificant amounts of uranium were found.

Five fire fighters and one health physicist wearing self-contained oxygen supplies entered the room. They developed skin irritation with erythema of the exposed portion of the body. They were treated by showers and application of magnesium oxide paste. By the next morning the irritation and erythema had disappeared. Ten other men inhaled varying amounts of fumes. Of these four vomited; none developed pulmonary edema or signs or symptoms of lung damage.

Interest in the local treatment of hydrofluoric burns was stimulated by this case. It was found that the application of concentrated hydrofluoric acid to the flexor surface of the forearm would cause a minimal burn if left in contact with the skin for 15 sec.

A drop of concentrated hydrofluoric acid at room temperature was placed on the skin of the flexor surface of both forearms of one subject with a wax-coated wooden applicator stick and left there for 15 sec. The acid on the left arm was washed off by pouring 250 ml of water over it. That on the right arm was removed with 250 ml of a solution of 1 part borax, 1 part boric acid, and 22 parts water. A round, slightly elevated area of erythema developed at each site where a drop of hydrofluoric acid had been placed. These areas were of the same size, elevation, and color. They reached their maximum in about 8 hr and had cleared without blister formation in about 48 hr.

Concentrated hydrofluoric acid diluted with water in equal parts caused no visible burn when removed with water in 15 sec.

The above technique was again used, but with the time interval before washing increased to 20 sec. Concentrated hydrofluoric acid was applied to five spots on each forearm and after 20 sec each drop was washed away with a different substance. The first drop was washed with 200 ml of distilled water, the second with 200 ml of saturated magnesium sulfate, the third with 200 ml of the boric acid solution, the fourth with 200 ml of 3% calcium gluconate suspension, and the fifth with 3% sodium bicarbonate solution. After the wash the burns of the right arm were blotted dry and left exposed. Those on the left arm were covered with a wet dressing of the same material used in each case to wash the drop away. There was no significant difference between the lesions treated with soaks and those left exposed, nor did it make much difference which wash was used to remove the hydrofluoric acid.

Water appears to be just as effective for the removal of *unabsorbed* hydrofluoric acid from the skin as the other materials tested. Removal with water can easily be done in most laboratories within 20 sec. If neutralizing or complexing solutions are stocked, the time lost in fetching and using them will in most instances be greater than the time required for immediate removal by water.

R.A. Love

HOSPITAL DIVISION

Studies on the Relation of Sodium to the Hypertensive Process (6320)

Studies on the relation of sodium to the hypertensive process have been continued. During the past year the effect on blood pressure of drastic weight loss and gain in association with variation in salt intake has been studied in about a dozen humans. A variety of metabolic and isotopic studies have been made during the changes in weight, in an effort to relate changes in body composition to change in blood pressure.

L.K. DAHL, L. SILVER, AND R.W. CHRISTIE

Respiratory Studies on Rat Aorta and Rat Tail Tendon (6120)

Respiratory studies on rat aorta and rat tail tendon have been made as part of the study of blood vessel metabolism and the tissue components in blood vessels [*J. Exptl. Med.* **106**, 357 (1957)]. Such studies are being continued. The study of small blood vessels has made necessary the use of micromethods of analysis; for this purpose activation analysis has been begun on such tissues and promises to open up new vistas in this field. R.W. CHRISTIE, L. SILVER, AND L.K. DAHL

Studies on the Effect of Electrolytes on Connective Tissue Metabolism (6120)

The effects on connective tissue of changes in salt and caloric ingestion are being investigated in both patients and laboratory animals. Metabolism of ground substance is being followed by determinations of urinary acid mucopolysaccharide excretion in patients on various levels of sodium chloride ingestion.

Ion-binding capacity of ground substance has been measured in relation to sodium metabolism in the connective tissues of blood vessels and tail tendon of the rat. The influence of salt-active hormones on this system is also under study.

L. SILVER AND L.K. DAHL

Publications

Dissimilarity in Oxygen Consumption Between the Thoracic and Abdominal Aorta in Rats. R.W. Christie and L.K. Dahl. *J. Exptl. Med.* **106**, 357 (1957).